# (19) World Intellectual Property Organization International Bureau



## 1 1886 BRITARI I REBRIT BERRI BERRI KERIN IN 1881 BRITA BERRI BERRI BERRI BERRI BERRI BERRI BERRI BERRI BERRI

## (43) International Publication Date 7 December 2000 (07.12.2000)

### **PCT**

# (10) International Publication Number WO 00/72880 A3

(51) International Patent Classification<sup>7</sup>: A61K 39/395, 38/17, 39/39, 39/00, G01N 33/68, Λ61K 48/00, Λ61P 25/28 // C07K 16/18, 14/47

(21) International Application Number: PCT/US00/14810

(22) International Filing Date: 26 May 2000 (26.05.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

09/322,289

28 May 1999 (28.05.1999) U

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:

US Filed on 09/322,289 (CIP) 28 May 1999 (28.05.1999)

(71) Applicant (for all designated States except US): NEU-RALAB LIMITED [—/—]; 102 St. James Court, Flatts, Smiths FL04 (BM).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SCHENK, Dale, B. [US/US]; 1542 Los Altos Drive, Burlingame, CA 94010 (US). BARD, Frederique [FR/US]; 1111 Park Pacifica Avenue, Pacifica, CA 94404 (US). VASQUEZ, Nicki, J. [US/US]; 310 Sanchez Street, San Francisco, CA 94114

(US). YEDNOCK, Ted [US/US]; 184 Arroyo Road, Forest Knolls, CA 94933 (US).

- (74) Agents: LJEBESCHUETZ, Joc et al.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published:

With international search report.

(88) Date of publication of the international search report: 31 May 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PREVENTION AND TREATMENT OF AMYLOIDOGENIC DISEASE

(57) Abstract: The invention provides improved agents and methods for treatment of diseases associated with amyloid deposits of  $A\beta$  in the brain of a patient. Such methods entail administering agents that induce a beneficial immunogenic response against the amyloid deposit. The methods are useful for prophylactic and therapeutic treatment of Alzheimer's disease. Preferred agents including N-terminal fragments of  $A\beta$  and antibodies binding to the same.



### INTERNATIONAL SEARCH REPORT

Internal J Application No PCT/US 00/14810

| A VAN GOOL W A ET AL: "Concentrations of anyloid-beta protein in cerebrospinal fluid increase with age in patients free from neurodegenerative disease."  NEUROSCIENCE LETTERS, vol. 172, no. 1-2, 1994, pages 122-124, XP000961282 ISSN: 0304-3940 the whole document  P,X  SCHENK D ET AL: "Immunization with anyloid-beta attenuates Alzheimer -disease-like pathology in the PDAPP mouse 'see comments!"  NATURE, (1999 JUL 8) 400 (6740) 173-7. XP002154168 the whole document  P,X  WO 99 27944 A (SCHENK DALE B; ATHENA NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples claims |          |  | PC1/US 00/14810 | ·          |
|--|----------|--|-----------------|------------|
| A VAN GOOL W A ET AL: "Concentrations of amyloid-beta protein in cerebrospinal fluid increase with age in patients free from neurodegenerative disease."  NEUROSCIENCE LETTERS, vol. 172, no. 1-2, 1994, pages 122-124, XP000961282 ISSN: 0304-3940 the whole document  P,X SCHENK D ET AL: "Immunization with amyloid-beta attenuates Alzheimer -disease-like pathology in the PDAPP mouse 'see comments!."  NATURE, (1999 JUL 8) 400 (6740) 173-7. , XP002154168 the whole document  P,X WO 99 27944 A (SCHENK DALE B ;ATHENA NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples       |          |  | Onlowed to      | o claim No |
| amyloid-beta protein in cerebrospinal fluid increase with age in patients free from neurodegenerative disease." NEUROSCIENCE LETTERS, vol. 172, no. 1-2, 1994, pages 122-124, XP000961282 ISSN: 0304-3940 the whole document   P,X  SCHENK D ET AL: "Immunization with amyloid-beta attenuates Alzheimer -disease-like pathology in the PDAPP mouse 'see comments!."  NATURE, (1999 JUL 8) 400 (6740) 173-7. XP002154168 the whole document  P,X  WO 99 27944 A (SCHENK DALE B;ATHENA NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples   | Caregory | Guarden of Goodment, min materior, minere appropriate, or into recevant passages   | relevant to     | ciann NO.  |
| amyloid-beta attenuates Alzheimer -disease-like pathology in the PDAPP mouse 'see comments!." NATURE, (1999 JUL 8) 400 (6740) 173-7., XP002154168 the whole document  P,X WO 99 27944 A (SCHENK DALE B ; ATHENA NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples   | Α .      | amyloid-beta protein in cerebrospinal fluid increase with age in patients free from neurodegenerative disease."  NEUROSCIENCE LETTERS, vol. 172, no. 1-2, 1994, pages 122-124, XP000961282 ISSN: 0304-3940 | 1-              | 108        |
| NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples   | Ρ,Χ      | amyloid-beta attenuates Alzheimer -disease-like pathology in the PDAPP mouse 'see comments!." NATURE, (1999 JUL 8) 400 (6740) 173-7., XP002154168  | 48              | -86        |
|  | P,X      | NEUROSCIENCES INC (US)) 10 June 1999 (1999-06-10) examples   |                 | 108        |

### INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna al Application No PCT/US 00/14810

| Patent document<br>cited in search report | :   | Publication date |                            | atent family<br>member(s)                                     | Publication date   |
|---|-----|------------------|----------------------------|---|--|
| EP 0613007                                | Α   | 31-08-1994       | CA<br>JP                   | 2115900 A<br>6294798 A  | 23-08-1994<br>21-10-1994   |
| WO 9511994                                | A . | 04-05-1995       | US<br>AU<br>AU<br>AU<br>CA | 5604102 A<br>8079894 A<br>702293 B<br>8080994 A<br>2174429 A  | 18-02-1997<br>22-05-1995<br>18-02-1999<br>22-05-1995<br>04-05-1995 |
| •   |     |                  | CA<br>EP<br>EP<br>EP       | 2174632 A<br>2174632 A<br>0736106 A<br>0730643 A<br>1001019 A | 04-05-1995<br>04-05-1995<br>09-10-1996<br>11-09-1996<br>17-05-2000 |
|   |     |                  | JP<br>JP<br>WO             | 9508196 T<br>9507746 T<br>9511968 A                           | 19-08-1997<br>12-08-1997<br>04-05-1995                             |
|   |     |                  | US<br>US                   | 5612486 A<br>5850003 A  | 18-03-1997<br>15-12-1998   |
| WO 9927944                                | Α   | 10-06-1999       | BR<br>EP<br>NO<br>AU       | 9815357 A<br>1033996 A<br>20002784 A<br>1706199 A             | 24-10-2000<br>13-09-2000<br>31-07-2000<br>16-06-1999               |

### INTERNATIONAL SEARCH REPORT

| Application No PCT/US 00/14810

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K39/395 A61K38/17

A61K48/00

A61P25/28

A61K39/39 A61K39/00 //C07K16/18,C07K14/47

G01N33/68

According to International Patent Classification (IPC) or to both national classification and IPC

#### **B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

STRAND, MEDLINE, LIFESCIENCES, CANCERLIT, AIDSLINE, CHEM ABS Data, EMBASE, SCISEARCH, WPI Data, EPO-Internal, PAJ, BIOSIS

| ent, with indication, where appropriate, of the relevant passages             | Relevant to claim No.   |
|---|---|
|   | Total to stall to.  |
| TENCES INC (US))<br>st 1994 (1994-08-31)<br>l, line 46 -column 2, line 4      | 1-52,<br>87-108   |
| IENCES INC (US))<br>995 (1995-05-04)<br>line 7-13<br>line 31 -page 6, line 18 | 100-108   |
|   | 3 007 A (LILLY CO ELI ;ATHENA IENCES INC (US)) st 1994 (1994-08-31) l, line 46 -column 2, line 4 5, line 27 -column 8, line 18  1994 A (LILLY CO ELI ;ATHENA IENCES INC (US)) 995 (1995-05-04) line 7-13 line 31 -page 6, line 18 , line 23 -page 19, line 30 |

| Special categories of cited documents: |  |  |
|--|--|--|

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international titing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document reterring to an oral disclosure, use, exhibition or other means
- document published prior to the international filling date but later than the priority date claimed
- "T" later document published after the international filing date or priority date and not in conflict with the application but clied to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled

Date of mailing of the international search report

\*&\* document member of the same patent family

Date of the actual completion of the international search

15/12/2000

29 November 2000 Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentiaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016

Authorized officer

Covone, M

1